PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
TERESA A. LAVOIE
FISH & RICHARDSON P.C.
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

	Date of mailing *(day/month/year)* **05 MAR 2010**
Applicant's or agent's file reference 253240028WO1	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 10/20259	International filing date *(day/month/year)* 06 January 2010 (06.01.2010)
Applicant CUREMARK LLC	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 338 8270

   For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30** months from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 253240028WO1	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US 10/20259	International filing date *(day/month/year)* 06 January 2010 (06.01.2010)	(Earliest) Priority Date *(day/month/year)* 06 January 2009 (06.01.2009)
Applicant CUREMARK LLC		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

3. ☐ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

COMPOSITIONS AND METHODS FOR THE TREATMENT OR THE PREVENTION oral INFECTIONS by E. COLI

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 10/20259

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 17/00 (2010.01)
USPC - 530/350
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - C07K 17/00 (2010.01)
USPC - 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 424/400

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST (PGPB,USPT,USOC,EPAB,JPAB), Google Scholar: protease, $protease, amylase, papain, lipase, $amylase, $lipase, trypsin, $trypsin, digestive enzyme, composition, infection, pharmaceutical, drug, treat, treatment, treating, treated, therap$, administ$, diarrhea, antiseptic, detergent, antimicrobial

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y	US 2006/0105379 A1 (WU et al.) 18 May 2006 (18.05.2006) para [0025]; [0038]; [0149]-[0150]; [0489]; [0723]; [0725]; [1104]	17-21, 26, 28 ---------- 1-16
X ---- Y	US 2008/0317731 A1 (GRAMATIKOVA et al.) 25 December 2008 (25.12.2008) para [0590]; [0593]-[0594]; [0598]; [0600]	22-23, 25, 29-31 ---------- 24
Y	US 2006/0259995 A1 (CAYOUETTE et al.) 16 November 2006 (16.11.2006) para [0001]; [0011]; [0034]; [0049]-[0050]; [0105]; [0121]; [0132]; [0325]; [0474]-[0476]; [0498]; [0513]-[0515]; [0517]; abstract	1-16, 24, 27
Y	US 2004/0076590 A1 (WILKINS J.) 22 April 2004 (22.04.2004) abstract; para [0015]-[0016]; Tables 1-2	27
Y	US 6,280,726 B1 (WEINRAUCH et al.) 28 August 2001 (28.08.2001) col 2, ln 5-11; col 10, ln 35 -45	8
Y	US 2005/0187130 A1 (BOOKER et al.) 25 August 2005 (25.08.2005) para [0037]	10-11

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
05 February 2010 (05.02.2010)	05 MAR 2010
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: TERESA A. LAVOIE
FISH & RICHARDSON P.C.
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	05 MAR 2010

Applicant's or agent's file reference	FOR FURTHER ACTION
253240028WO1	See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 10/20259	06 January 2010 (06.01.2010)	06 January 2009 (06.01.2009)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - C07K 17/00 (2010.01)
USPC - 530/350

Applicant CUREMARK LLC

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	05 February 2010 (05.02.2010)	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/237 (cover sheet) (July 2009)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/20259

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification** of an **obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:

   a. (means)

      ☐ on paper

      ☐ in electronic form

   b. (time)

      ☐ in the international application as filed

      ☐ together with the international application in electronic form

      ☐ subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/20259

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-16, 24, 27	YES
	Claims	17-23, 25-26, 28-31	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-31	NO
Industrial applicability (IA)	Claims	1-31	YES
	Claims	NONE	NO

2. Citations and explanations:

Claims 17-21, 26 and 28 lack novelty under PCT Article 33(2) as being anticipated by US 2006/0105379 A1 to Wu et al. (hereinafter "Wu").

Regarding claim 17, Wu teaches a method of treating a mammal exhibiting one or more symptoms of an E. coli infection comprising administering to the mammal a therapeutically effective amount of a composition comprising one or more digestive enzymes (para [0038], [0025] and [0150]).

Regarding claim 18, Wu teaches administering a beta-lactam antibiotic to the mammal (para [1104] and [0038]).

Regarding claim 19, Wu teaches a method for treating diarrhea in an individual (para [0149]), comprising administering a pharmaceutical composition comprising one or more digestive enzymes to the individual (para [0038], [0025] and [0149]).

Regarding claim 20, Wu teaches the individual is diagnosed with an E. coli infection (para [0150] and [0723]).
Regarding claim 21, Wu teaches the E. coli is a STEC (para [0150] and [0725]).

Regarding claim 26, Wu teaches a method for reducing the amount of E. coli present on a skin region, tissue, or wound of a mammal comprising applying to the skin region, tissue, or wound a composition comprising one or more digestive enzymes (para [0150], [0489] and [0038]).

Regarding claim 28, Wu teaches an antibiotic comprising one or more digestive enzymes, wherein the antibiotic is bacteriocidal for E. coli (para [1104], [0150] and [0105]).

Claims 22-23, 25 and 29-31 lack novelty under PCT Article 33(2) as being anticipated by US 2008/0317731 A1 to Gramatikova et al. (hereinafter "Gramatikova").

Regarding claim 22, Gramatikova teaches a method for sanitizing or disinfecting a surface to reduce the amount of E. coli thereon or to eradicate the E. coli thereon (para [0593]-[0594] and [0598]), comprising applying to the surface a composition comprising one or more digestive enzymes (para [0593]-[0594]).

Regarding claim 23, Gramatikova teaches the surface is a nonliving or inanimate surface (para [0594]).
Regarding claim 25, Gramatikova teaches the surface is a food (para [0590] and [0600]).

Regarding claim 29, Gramatikova teaches a detergent comprising one or more digestive enzymes, wherein the detergent is bacteriocidal for E. coli (para [0593]-[0594] and [0598]).

Regarding claim 30, Gramatikova teaches an antiseptic comprising one or more digestive enzymes, wherein the antiseptic is bacteriocidal for E. coli (para [0593]-[0594] and [0598]).

Regarding claim 31, Gramatikova teaches a disinfectant comprising one or more digestive enzymes, wherein the disinfectant is bacteriocidal for E. coli (para [0593]-[0594] and [0598]).

(continued in next supplemental box)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/20259

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
(citations and explanations from box V.2)

Claims 1-7, 9 and 12-16 lack an inventive step under PCT Article 33(3) as being obvious over US 2006/0259995 A1 to Cayouette et al. (hereinafter "Cayouette") in view of Wu.

Regarding claim 1, Cayouette teaches a method for the treatment of a bacterial infection in a mammal, comprising administering to the mammal a therapeutically effective amount of a pharmaceutical composition comprising one or more digestive enzymes (para [0105] and [0034]).
Cayouette does not specifically teach the bacteria is E. coli. Wu teaches a method for the treatment of an E. coli. infection in a mammal, comprising administering to the mammal a therapeutically effective amount of a pharmaceutical composition comprising a digestive enzyme (para [0025], [0038] and [0150]). It would have been obvious to one of ordinary skill in the art to have performed a method for the treatment of an E. coli infection as claimed, in view of Cayouette teaching the composition comprising digestive enzymes with protease activity including metalloprotease activity as an antimicrobial agent (para [0001] and [0034]), and is used to treat bacterial infections (para [0105]), since Wu teaches a composition comprising metalloprotease to treat an E. coli infection (para [0025], [0038] and [0150]), and a person of ordinary skill in the art would have readily appreciated use of the method taught by Cayoutte to treat the bacterial infections taught by Wu since the same enzymatic activity is utilized.

Regarding claim 2, Cayouette teaches the one or more digestive enzymes comprise one or more enzymes selected from the group consisting of proteases, amylases, papain, and lipases (para [0034] and [0121]).

Regarding claim 3, Cayouette teaches the one or more digestive enzymes comprise one or more pancreatic enzymes (para [0034] and [0132]).

Regarding claim 4, Cayouette teaches the one or more of the digestive enzymes comprise pig enzymes (para [0049] and [0325]).
Regarding claim 5, Cayouette teaches the proteases comprise chymotrypsin and trypsin (para [0034]).

Regarding claim 6, Cayouette teaches the one or more digestive enzymes are, independently, derived from an animal source, a microbial source, a plant source, or a fungal source (para [0011] and [0049]-[0050]).

Regarding claim 7, Cayouette teaches the mammal is a human (para [0498] and [0105]).

Regarding claim 9, Cayouette teaches the composition comprises at least one amylase (para [0121]), a mixture of proteases comprising chymotrypsin and trypsin (para [0034]), and at least one lipase (para [0121]).

Regarding claim 12, Cayouette teaches the composition is a dosage formulation selected from the group consisting of: creams, lotions, aerosols, powders, liquids, gels, and a combination of any thereof (para [0105] and [0474]).

Regarding claim 13, Cayouette teaches the composition is formulated for oral administration (para [0105]).
Regarding claim 14, Cayouette teaches the composition is formulated for topical administration (para [0105]).
Regarding claim 15, Wu teaches the composition is effective against STEC (para [0150], [0723] and [0725]).
Regarding claim 16, Wu teaches the composition is effective against ETEC (para [0723] and [0725]).

Claim 24 lacks an inventive step under PCT Article 33(3) as being obvious over Gramatikova, as above, in view of Cayouette.

Regarding claim 24, Gramatikova does not specifically teach the surface is on a medical device. Cayouette teaches a method for sanitizing or disinfecting a surface to reduce the amount of bacteria thereon (para [0474]-[0476] and [0513]-[0515]), wherein the surface is on a medical device (para [0517]). It would have been obvious to one of ordinary skill in the art to have performed a method for sanitizing or disinfecting a surface as claimed, wherein the surface is on a medical device, in view of Gramatikova teaching disinfecting a surface (para [0594]), since Cayouette teaches a method of disinfecting a medical device surface (para [0517]), and a person of ordinary skill in the art would have readily appreciated use of the sanitization method taught by Gramatikova on the surface of a medical device as taught by Cayouette, to prevent contamination of patients with said device.

Claim 27 lacks an inventive step under PCT Article 33(3) as being obvious over Cayouette, as above, in view of US 2004/0076590 A1 (Wilkins).

Regarding claim 27, Cayouette teaches a disinfectant comprising one or more digestive enzymes (abstract and para [0515]). Cayouette does not specifically teach the disinfectant has a phenol coefficient of >1 to about 20 for S. aureus or E. coli. Wilkins teaches a disinfectant having a phenol coefficient of >10 for S. aureus and E. coli (para [0015], [0016], Tables 1 and 2), wherein determination of a phenol coefficient can be achieved via a standard phenol coefficient assay (para [0015]). It would have been obvious to one of ordinary skill in the art to have provided a disinfectant as claimed, wherein the disinfectant has a phenol coefficient of >10 for S. aureus or E. coli., in view of Cayouette teaching the disinfectant comprising one or more active digestive enzymes with antimicrobial properties (para [0105], [0513] and [0034]), and in light of Wilkins teaching obtaining a phenol coefficient of >10 for S. aureus and E. coli. for a disinfectant composition effective to reduce or eliminate microbes (abstract, para [0015], [0016], Tables 1 and 2), since a person of ordinary skill in the art would have readily appreciated how to achieve the claimed a phenol coefficient by ordinary experimentation with the antimicrobial elements of the composition.

********** continued in next supplemental box **********

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 10/20259

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
Box V(2) and the preceding Supplemental Box:

Claim 8 lacks an inventive step under PCT Article 33(3) as being obvious over Cayouette in view of Wu, as above, and further in view of US 6,280,726 B1 to Weinrauch et al. (hereinafter "Weinrauch").

Regarding claim 8, Cayouette does not specifically teach the animal source is a pig pancreas. However, Cayouette does teach the source is a recombinant pig tissue sample (para [0049] and [0325]), and the enzymes are pancreatic enzymes (para [0034] and [0132]). Weinrauch teaches a composition comprising digestive enzymes isolated from an animal source, wherein the animal source is a pig pancreas (col. 5, ln 2-27 and col. 10, ln 35-45). It would have been obvious to one of ordinary skill in the art to have performed a method for the treatment of a bacterial infection in a mammal as claimed, wherein the animal source of the enzyme is a pig pancreas, in view of Cayouette teaching the source is a pig tissue sample (para [0049] and [0325]), and the enzymes are pancreatic enzymes (para [0034] and [0132]), since Weinrauch teaches the composition comprising digestive enzymes isolated from a pig pancreas comprises recombinantly produced proteases (col. 2, ln 5-11 and col. 10, ln 35-45), and a person of ordinary skill in the art would have readily appreciated isolation of the protease taught by Cayouette in view of Wu, from a pig pancreas as taught by Weinrauch, since Weinrauch teaches recombinant pigs producing protease in the pancrease.

Claims 10-11 lack an inventive step under PCT Article 33(3) as being obvious over Cayouette in view of Wu, as above, and further in view of US 2005/0187130 A1 to Booker et al. (hereinafter "Booker").

Regarding claim 10, Cayouette does not specifically teach the pharmaceutical composition comprises at least one protease and at least one lipase (para [0034] and [0121]). Cayouette does not specifically teach the ratio of total proteases to total lipases (in USP units) ranges from about 1:1 to about 20:1. However, Cayouette does teach compositions comprising varying relative amounts of at least one protease and at least one lipase (para [0034], [0474] and [0121]). Booker teaches a composition compnsing at least one protease and at least one lipase, wherein the ratio of total proteases to total lipases ranges from about 1.5:1 to about 3:1 (para [0037]). It would have been obvious to one of ordinary skill in the art to have provided a pharmaceutical composition as claimed, wherein the ratio of total proteases to total lipases ranges from about 1:1 to about 20:1, in view of Cayouette teaching compositions comprising varying relative amounts of at least one protease and at least one lipase for use as antimicrobial agents in pharmaceuticals and detergents (abstract, para [0034], [0474] and [0121]), and in light of Booker teaching a detergent composition comprising at least one protease and at least one lipase, wherein the ratio of total proteases to total lipases ranges from about 1.5:1 to about 3:1 (para [0037]), since a person of ordinary skill in the art would have readily appreciated use of the protease to lipase ratio taught by Booker in the composition taught by Cayouette in view of Wu, since Booker teaches this ratio is effective for utilizing the enzymatic activity.

Regarding claim 11, Booker teaches the pharmaceutical composition comprises at least one protease and at least one lipase, and wherein the ratio of total proteases to total lipases (in USP units) is about 4: 1 (para [0037] - a ratio of about 3:1 is about 4:1).

Claims 1-31 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in the industry.